Syndrome of the month

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FG syndrome

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The individual clinical features of the FG syndrome are non-specific and the dysmorphology is subtle, but together they form the pattern first recognised by Opitz and Kaveggia in 1974.[1] They described the syndrome in three brothers and two of their male first cousins who had mental retardation, relative macrocephaly, imperforate anus, and congenital hypotonia, and they named the condition using the first letter of the surnames in the two branches of the family. A further 26 cases have since been reported.[2–8]

Major clinical features

(1) Mental retardation which is usually severe.
(2) Characteristic facial appearance due to hypotonia, giving a droopy, 'open-mouthed' expression, a thin upper lip, and full 'pouting' lower lip. Upsweep of the hair line ('cowlicks'), broad, tall forehead, hypertelorism, deep set eyes, large appearing corneae, and a long philtrum are frequently present. Medial epicanthus and sparse hair also appear to be common.
(3) Severe congenital hypotonia.
(4) Relative macrocephaly.
(5) Severe chronic constipation with or without structural anal anomalies (imperforate anus, anal stenosis, anal skin tags, and anteriorly placed anus).
(6) Failure to thrive and ultimate short stature are common. Occasionally normal or tall stature is seen.
(7) Death in infancy, usually from respiratory infection, has occurred in about one-third of previously reported cases. However, once the patient has survived infancy, death is rare.
(8) Hyperactive behaviour. Many have an outgoing, friendly personality, punctuated in some by bursts of aggression.

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Other anomalies less commonly associated with the FG syndrome

CNS: epilepsy or abnormal EEG, strabismus, hearing loss, agenesis of corpus callosum.[9]
GIT: pyloric stenosis, malrotation, herniae.
Skeletal: joint contractures, broad thumbs and halluces, short fingers and toes.

TABLE 1 *Major manifestations of the FG syndrome.*

	11 patients (personally seen, not previously reported)	*31 patients (previously reported)*	*Total 42 patients*	%
(1) Mental retardation	11/11*	24/24	35/35	100
(2) Facial appearance				
Broad, tall forehead	10/11	22/22	32/33	97
Cowlicks of hairline	11/11	15/18	26/29	90
(3) Congenital hypotonia	9/11	22/24	31/35	89
(4) Relative macrocephaly	7/11	18/24	25/35	71
(5) Constipation	9/11†	16/25	25/36	69
(6) Anal anomaly	1/11‡	15/31	16/42	38
(7) Failure to thrive	6/11	16/22	22/33	67
(8) Death in infancy	1/11	12/29	13/40	33
(9) Hyperactive behaviour	6/11	12/24	18/35	51

* Retardation is usually severe. One patient (patient 4) only mildly retarded. His affected brother (patient 3) is severely retarded. † Constipation severe in seven patients (regular laxatives or enemas needed). Investigations for Hirschsprung's disease in patient 7 negative. Constipation less severe in two patients. ‡ One patient (patient 7) had anal stricture. Previously reported cases had imperforate anus, anal stenosis, or anal tags. This table does not include anteriorly placed anus alone.

TABLE 2 *Some other anomalies associated with the FG syndrome.*

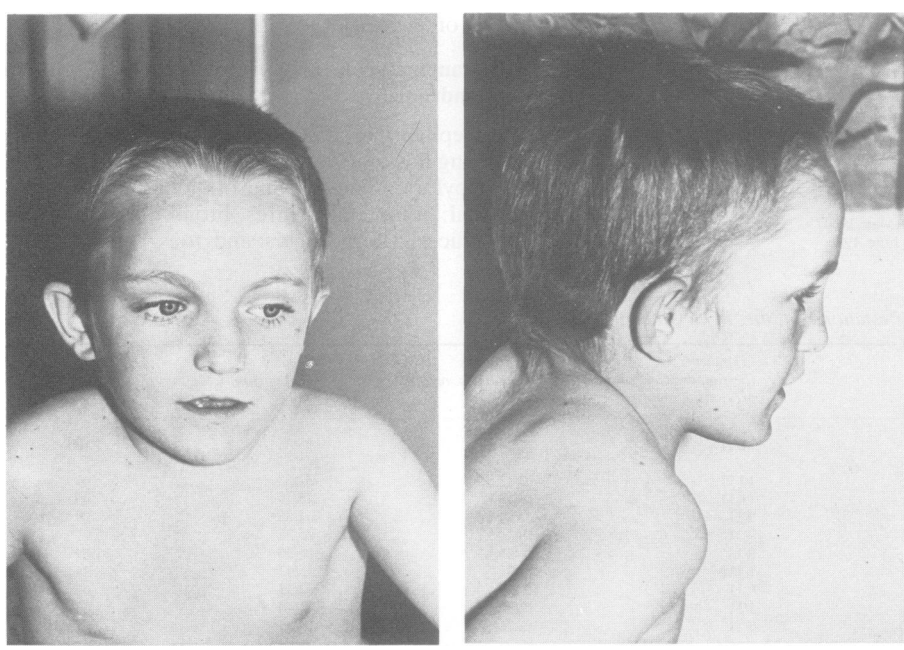
	11 patients (personally seen, not previously reported)	*31 patients (previously reported [1–8])*	*Total 42 patients*	%
Broad thumbs and halluces	5/7	15/18	20/25	80
Dysplastic pinnae*	5/11	14/20	19/31	61
Fine, sparse hair	7/11	4/7	11/18	61
Prominent fetal pads or high whorl count on fingers and toes	5/11	8/11	13/22	59
Strabismus	5/11	5/8	10/19	53
Herniae	3/11	9/12	12/23	52
Joint contractures	4/11	7/17	11/28	39
Cryptorchidism	2/11	7/18	9/29	31
Hearing loss	1/11	6/11	7/22	32
Pyloric stenosis	1/11	2/31	3/42	7
Maternal carrier manifestations	4/8†	3/15	7/23	30

* Includes simple shape, overfolded helix, soft and protruding pinnae, and other minor anomalies.
†Three mothers had tall, broad foreheads, one with 'cowlicks'. One other mother had significant early learning difficulties.

Dermatoglyphics: prominent fetal pads on the ventral surface of the tips of fingers and toes with high digital whorl count, low total ridge count, ridges extending over distal interphalangeal flexion creases.
Genital: cryptorchidism, hypospadias, hydrocele.
Other: sacral dimple, minor anomalies of pinnae, congenital heart disease, craniosynostosis.

Congenital hypotonia probably accounts for manifestations such as the herniae, poor feeding in infancy, and recurrent respiratory infections, but probably does not entirely account for the severe constipation. Hypotonia also contributes to the facial appearance.

Since our report of seven new cases of the FG syndrome,[8] we have seen a further 11 affected



(a) *(b)*

FIG 1 *(a) Patient 1 (brother of patient 2). Note bilateral upsweeps ('cowlicks') of frontal hair line, tall, broad forehead, and hypertelorism. (b) Note the 'cowlick' of the posterior hair line, fine sparse hair, and well developed nasal bridge.*

males. The patients comprise three sib pairs, two first cousins, and three single cases. The common clinical features in these cases and in other reported cases are summarised in tables 1 and 2. The facial features of seven of these previously unpublished cases are shown in figs 1 to 8.

Inheritance

This is an X linked recessive disorder. Manifestations in some obligate carrier mothers have included a similar facial appearance to affected boys, with broad, tall forehead, hypertelorism, and 'cowlicks' of the hair line. Recurrent miscarriages in two mothers and congenital hypotonia in one of these were reported.[2–8] Mothers are generally intellectually normal.

Diagnosis

The diagnosis of the FG syndrome should be considered in mentally retarded males with severe congenital hypotonia, relative macrocephaly, and severe constipation with or without structural anal anomalies. The facial appearance is usually characteristic due to a high, broad forehead and cowlicks of the hair line with an open mouthed, 'drooping' expression. There is variability in presence and

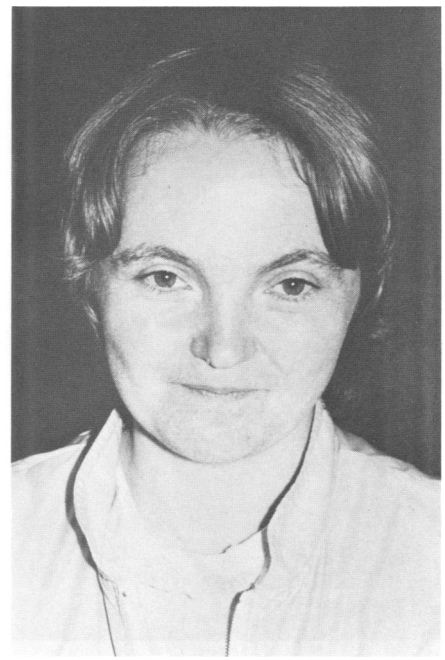


FIG 3 *Mother of patients 1 and 2. Note tall, broad forehead, bilateral 'cowlicks' of frontal hair line, and hypertelorism.*

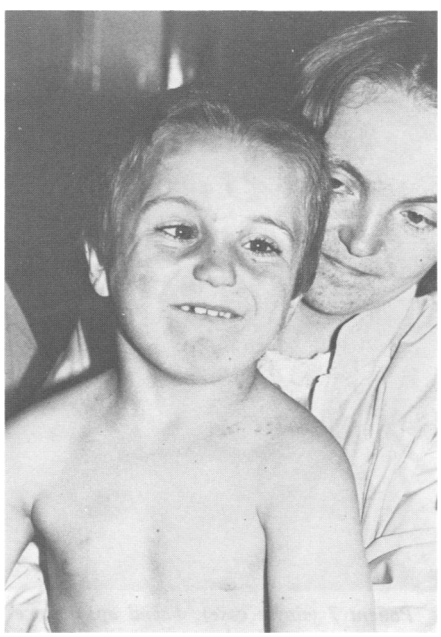


FIG 2 *Patient 2 (brother of patient 1). Note tall, broad forehead, bilateral frontal 'cowlicks', hypertelorism, and strabismus.*

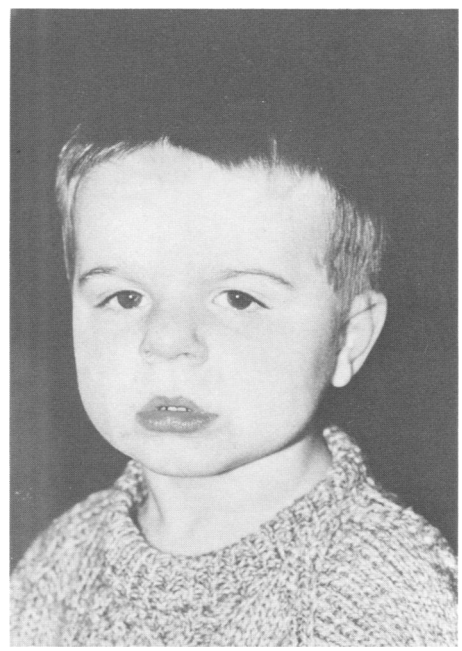


FIG 4 *Patient 3 (brother of patient 4). Note broad, tall forehead, 'cowlicks', thin upper lip with full pouting lower lip, and long philtrum.*

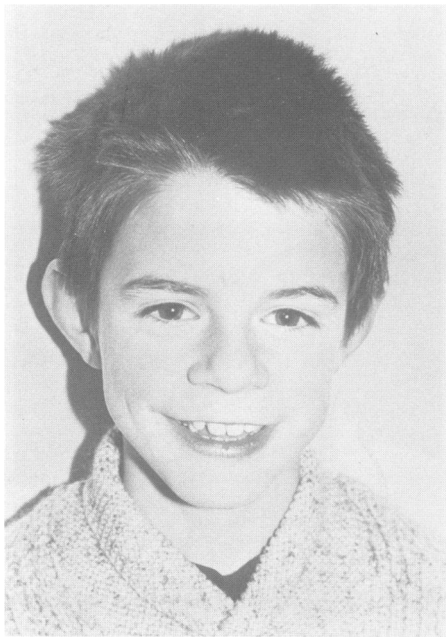


FIG 5 *Patient 4. Note right 'cowlick'. Patient more mildly affected than his brother (patient 3), with milder mental retardation and less pronounced facial changes.*

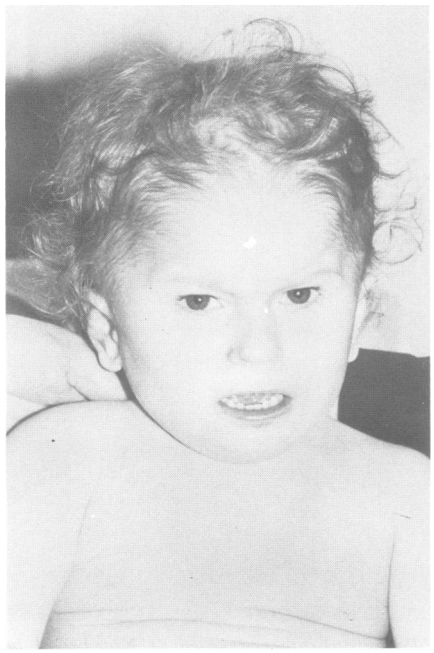


FIG 6 *Patient 5 (single case). Note fine sparse hair, upsweep of hair off forehead, and thin upper lip.*

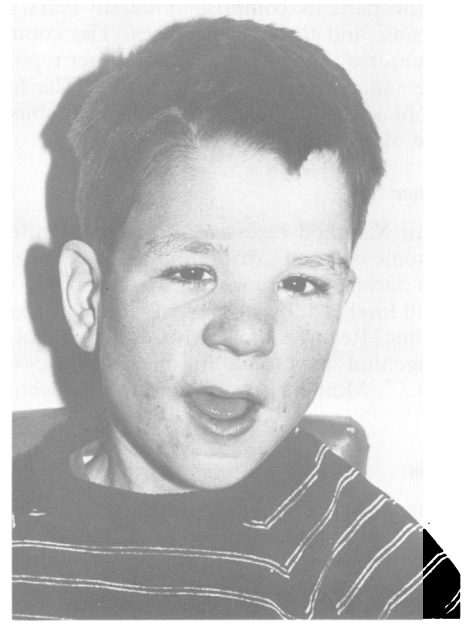


FIG 7 *Patient 6 (single case). Note open mouthed appearance, cowlicks, broad forehead, epicanthus, and long philtrum.*

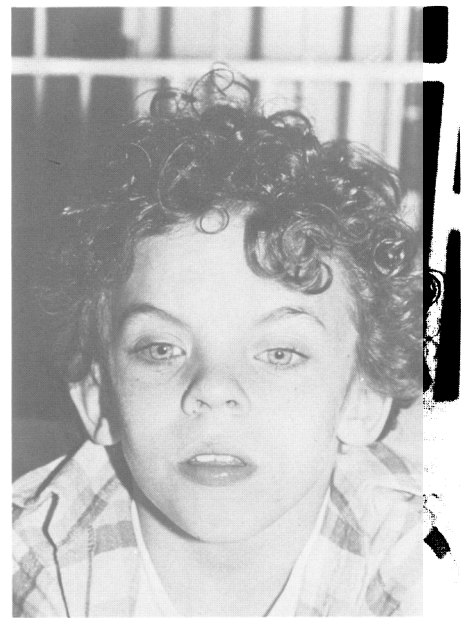


FIG 8 *Patient 7 (single case). Facial appearance of FG syndrome not as immediately apparent as in the other cases shown, but note open mouthed 'hypotonic' facial appearance, broad forehead, hypertelorism, and long philtrum.*

severity of these features which can make the diagnosis difficult in single cases. In addition, the typical facial appearance is more readily apparent in some cases (figs 1, 2, 4, 6, and 7) than others (figs 5 and 8).

It is important to look for fragile sites on the X chromosome in all suspected cases, since males with the commoner Martin-Bell syndrome may have macrocephaly and joint laxity. Males with the X linked Coffin-Lowry syndrome tend to have an open mouthed appearance with a prominent lower lip, but generally the facial features are coarser than in the FG syndrome. Tufted terminal phalanges and vertebral defects occur in the Coffin-Lowry syndrome.

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